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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
JUEDES, AMY E	
ART UNIT	PAPER NUMBER
1644	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,813	FRASER, JOHN DAVID	
	Examiner	Art Unit	
	Amy E. Juedes, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *5,6,8,9,14-17 and 21-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7,10-13 and 18-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of group I, drawn to an immunomodulator comprising a superantigen, claims 1-13 and 18-22, in the reply filed on 8/31/07, is acknowledged. Applicant has further elected the superantigen comprising mutation D42C as the species of superantigen, and ovalbumin as the species of antigen. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 14-17 and 23-28 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 5-6, 8-9, and 21-22 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species. It is noted that Applicant asserts that claims 5-6 and 21-22 read on the elected species. Applicant was required to elect a specific immunomodulator comprising a specific mutation or combination of mutations. Applicant elected the D42C mutation. Claims 5-6 and 21-22 are drawn to an immunomodulator or a superantigen comprising a specific combination of multiple different mutations, and do not read on the elect species of a superantigen/immunomodulator comprising only the D42C mutation.

Claims 1-4, 7, 10-13, and 18-20 read on the elected invention and are being acted upon.

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 7, 10-13, and 18-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) The terms "immunomodulator" and "immunomodulatory" in claims 1-4, 7, 10-13, and 18 are indefinite because it is not clear what direction, type, or degree of immunomodulation is required. The terms immunomodulator or immunomodulatory could be interpreted in a variety of ways. For example, it might indicate an increase or decrease in an immune response, or it could indicate that a particular type of immune response is turned on or off. In addition, said immunomodulation could be intermittent, or constant. Since the instant specification does not define the meaning of immunomodulate, it not clear what degree, direction, or type of immunomodulation is required.

B) Additionally, the terms "fully functional" in Claim 1 and "little or no ability" in Claim 2 are relative terms which render the claims indefinite. The recitation of "little" as pertaining to ability of a superantigen to activate T cells is vague. It is known that disruption of superantigen T cell receptor binding sites can result in reduced ability to stimulate only certain subsets of T cells, while being fully functional to stimulate other subsets. It is unclear whether a superantigen with such a disruption might reasonably be considered to have a "little" ability to activate T cells. Furthermore, disruption of the T cell receptor binding site may result in a wide range of effects on the ability of a superantigen to stimulate T cells. For example, a disruption that results in a 10,000 fold reduction in T cell stimulatory capacity would be considered to have "little" ability to activate T cells. However, it is not defined by the claim or the specification if a modification that resulted in, for example, only a 2 fold reduction might also be considered to have "little" ability to activate T cells. Furthermore, the recitation of "fully functional" or "defective" T cell receptor binding site in Claims 1 and 7 is indefinite. Since a superantigen can bind T cells and/or stimulate T cells, it is unclear if the terms "defective" or "fully functional" relate to either or both of those functions. Likewise, the term "fully" is vague. It is not clear what degree of impairment is necessary to be considered not fully functional. Therefore, the claims as written do not define the metes and bounds of the invention.

C) Claims 3 and 19 are indefinite in the recitation of SMEZ superantigen having one or more mutations at positions 18, 42, 75, and 182 of SEQ ID NO: 1. The claims, as written, indicate that the SMEZ superantigen has one or more mutations at a single

amino acid residue (i.e. at position 18). An amino acid residue is either mutated or not, and it is unclear how a single amino acid can comprise multiple mutations. Are the claims intended to recite that the SMEZ superantigen comprises one or more mutations at positions 18, 42, 75 **or** 182 of SEQ ID NO: 1?

D) Claim 7 recites the limitation "the defective TCR binding SMEZ-2" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

E) Claim 19 is indefinite in the recitation a superantigen having "the SEQ ID NO: 1". It is unclear whether the claims are intended to encompass superantigens with *the sequence of* SEQ ID NO: 1, or any protein designated "SEQ ID NO: 1".

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 7, 10-13, and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant has not adequately disclosed that they are in possession of APC-targeting molecules that "mimic" SMEZ-2 or that are "structurally" a SMEZ-2, or molecules comprising a "defective TCR binding SMEZ-2".

The instant claims are drawn to an immunomodulator comprising an APC-targeting molecule that "mimics" or is "structurally" a SMEZ-2 superantigen, but for a disrupted TCR binding site. This might encompass a wide range of structurally and functionally different molecules. For example, the claims might encompass an antibody which is specific for MHC-II (i.e. "mimics" a SMEZ-2 superantigen). Said antibody might also be considered to be "structurally" a SMEZ-2 superantigen, since it comprises an MHC-II binding region. Additionally, the claims encompass any polypeptide that shares any degree of sequence

similarity with any SMEZ-2 superantigen. This might include peptide fragments of a SMEZ-2, or any number of mutations, additions, or deletions to any SMEZ-2 polypeptide. This would encompass a wide range of structurally different polypeptides with unique amino acid sequences. Furthermore, the only functional limitation of the claimed targeting molecules is that they have a defective/not fully functional/disrupted TCR binding site. Thus, the claims might even include targeting molecules that are not capable of binding to MHC, and "mimic" the ability of SMEZ to serve as an antigen to generate specific antibodies. Therefore, the genus encompassed by APC targeting molecules that "mimic" or a "structurally" SMEZ-2, or "defective TCR binding SMEZ-2" is extremely large, and might encompass a broad range of structurally and functionally different molecules. In contrast, Applicant has only disclosed the SMEZ-2 polypeptide of SEQ ID NO: 1 with mutations at residues 18, 42, 75, and/or 182. Thus, one of skill in the art would conclude that the specification fails to provide adequate written description to demonstrate that Applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F. 3d 1559, 43, USPQ2d 1398.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 7, 10-13, and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 02/45739 (of record), in view of Parks et al., 2002.

WO 02/45739 teaches an immunomodulator comprising a SMEZ-2 superantigen with a defective TCR binding site coupled to an antigen (see pages 3 and 15 in particular). WO 0245739 also teaches that residue D42 of SMEZ-2 is a critical residue for TCR binding that can be subjected to mutagenesis (see page 15 in particular). WO 02/45739 also teaches that it is useful to mutate TCR binding residues to cysteine in order to introduce a residue amenable to antigen coupling (see pages 18-19 in particular). WO 02/45739 also teaches coupling the antigen in a

reversible manner, and a pharmaceutical composition or vaccine comprising the immunomodulator (see pages 3-4, in particular),

WO 02/45739 does not teach the SMEZ-2 coupled to ovalbumin.

Parks et al. teach that ovalbumin is a well characterized model antigen comprising defined epitopes that is useful for studying the immune response to vaccination (see page 1167 in particular).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make the SMEZ-2 antigen conjugate taught by WO 02/45739, using ovalbumin as the antigen, as taught by Parks et al. The ordinary artisan at the time the invention was made would have been motivated to do so, and have a reasonable expectation of success, since Parks et al. teach that ovalbumin is a well characterized model antigen comprising defined epitopes that is useful for studying the immune response to vaccination.

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, Ph.D. whose telephone number is 571-272-4471. The examiner can normally be reached on 8am - 5pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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11/3/07
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